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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,022	09/17/2003	Dennis M. Klinman	4239-66899	7954

7590 12/06/2007

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EXAMINER
HORNING, MICHELLE S

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
12/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/666,022	KLINMAN ET AL.	
	Examiner	Art Unit	
	Michelle Horning	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22 and 25-28* is/are pending in the application.

4a) Of the above claim(s) *22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21 and 25-28* is/are rejected.

7)☒ Claim(s) *20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is responsive to communication filed 10/1/2007. The status of the claims is as follows: claims 1-21 and 25-28 are under current examination. Claim 22 is withdrawn as drawn to a non-elected invention.

The following rejections have been withdrawn due to amendments of the claims or accepted affidavits:

1. 35 USC 112, 1st paragraph;
2. 35 USC 102 (e) (Jiang et al);
3. 35 USC 102 (e) (Mond et al); and
4. 35 USC 102 (e) (Klinman et al).

Claim Objections

Claim 22 is objected to because of the following informalities: "retroviral" is repeated twice. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-17 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 7 recites Formula III and then provides SEQ ID NOs: 22-98. It is not clear whether these SEQ ID NOs are to be

read as merely examples of this formula or read as a general motif that is found in these SEQ ID NOs. Claims 8-17 and 26 depend on rejected claim 7. Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-21 and 25-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Enablement is considered in view of the *Wands* factors.

Nature of the invention. The claims are drawn to a method of increasing an immune response to an opportunistic infection in an immunocompromised subject via administration of an immunostimulatory D oligodeoxynucleotide.

State of the prior art. The prior art discloses that administration of CpG motifs in the plasmids of a DNA vaccine can stimulate normal human PBMC to produce IFN-gamma and IL-6 (Calarota et al, 1999). Further, CpG DNA has been shown to promote protection and resistance to leishmaniasis and Listeria (Krieg et al, 1998 and Walker et al, 1999).

Post filing art by the inventor makes the following recitation with respect to HIV-infected patients; this is noted for reasons of record. "However, HIV infection does not reduce the activity of the innate immune system until late in the disease process. So, PBMCs from retrovirus-infected primates (humans and mondkeys) continue to respond to CpG ODN stimulation" (see page 3, Klinman, 2004). Thus, there appears to be an intact immune system that is being stimulated by ODN's in the invention.

Breadth of the claims. Nearly all of the claims are extremely broad with respect to the immunocompromised states, the opportunistic infections and D-oligonucleotide sequences. These claims are drawn to any and all possible immunocompromised states and the opportunistic infections. Additionally, the claims are drawn to CpG-containing sequences which are highly variable. See claim 7 in which X and W are any nucleotide. Further, according to this formula M and N can be any integer from 0-10 or from 4 to 10.

Working examples. Working examples include SIV-infected monkeys with L. major treated with CpG ODN and mice with CGD disease with Listeria treated with CpG ODN. In vitro studies involved treating PBMC isolated from HIV-infected subjects with CpG ODN. No specific ODN's are provided in any of the working examples.

Please note that the following recitation is made on page 38: "Indeed, no single D or K CpG motif is optimally stimulatory in all donors. However, mixtures of ODNs were identified that strongly stimulated PBMC from all human donors. These D or K ODN mixtures were used in the in vivo studies in macaques." Verthelyi et al is cited but the mixture of ODN's used is not clear. The working examples do not provide which cocktail of ODNs were used for the macaques and which ODNs were used for the mice.

Predictability of the art. There is no way the ordinary artisan could predict a successful cocktail of ODNs that would achieve an increase in an immune of system to any and all opportunistic infections of any and all immunocompromised subjects. The specification provides a long list of opportunistic infections that a subject may be susceptible to, including genital herpes, cervical cancer and hepatitis (see pages 2 and 18, claims 15 and 17). Please note that L. major and Listeria are a protozoan and a bacterium; thus, they are not related. Additionally, immunocompromised subjects may include AIDS, diabetics, sickle cell anemia and many other diseased states. (see page 14).

Amount of experimentation necessary. Much experimentation is necessary to practice the full scope of the claimed method. Additional experimentation would include ascertaining which ODNs or mixtures thereof would be optimal for the numerous immunocompromised states in combination with the differential opportunistic infections. No guidance is given in the specification with respect as to which ODN's to use. It is not obvious from the specification that for example, a subject with cervical cancer would successfully exhibit an increase of an immune response to neoplasms or prions in response to any and all immunostimulatory D oligodeoxynucleotides or combinations thereof.

Conclusions

NO claim is allowed.

For the reasons above, it would require undue experimentation for one of ordinary skill in the art to practice the full scope of the claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michelle Horning whose telephone number is 571-272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michelle Horning
Patent Examiner

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